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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/892,981	06/27/2001	Roland Gerritsen van der Hoop	01722906	3783

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EXAMINER	
HUI, SAN MING R	
ART UNIT	**PAPER NUMBER**
1617	

DATE MAILED: 06/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/892,981	VAN DER HOOP, ROLAND GERRITSEN	
	Examiner	Art Unit	
	San-ming Hui	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 April 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,8-14 and 20-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,8-14, 20-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendments filed April 8, 2005 have been entered. Claims 1, 3, 8-14, and 20-23 are pending.

The outstanding rejection under 35 USC 112, second paragraph is withdrawn in view of the amendments filed April 8, 2005.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1,3,8-14, 20-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kaswan et al. (US Patent 5,639,743) in view of Carrara (US Patent 5,891,462) and Merck Index (11th ed., 1989, Monograph 5103).

Kaswan et al. teaches a method of administering androgen, such as methyltestosterone, and estrogen, such as estradiol, to treat vaginal gland atrophy in post-menopausal women to restore adequate amounts of exocrine gland fluid (See claims 1, 8, and 13, col. 4, line 50 to col. 5, line 5, col. 6, 63-66, and col. 7, lines 14-15). Kaswan et al. also teaches topical transdermal estradiol administration can minimize the first pass hepatic effect and that the recommended dosage administered as 0.3-1.25 mg per day (see col. 7, lines 56-60 and col. 8, lines 2-4). Kaswan et al. also teaches the dosage of oral methyltestosterone as 2-50mg per day (see col. 6, lines 63-66).

Kaswan et al. does not expressly teach the specific dosage forms of methyltestosterone and estradiol. Kaswan et al. does not expressly teach the herein claimed ingredients of the estradiol gel such as polyacrylic acid, triethanolamine, ethanol and isopropyl myristate. Kaswan et al. does not expressly teach methyltestosterone and estradiol being administered in sequential or simultaneous manner.

Carrara teaches a gel composition containing estradiol and the herein claimed ingredients (See claim 5). Carrara also teaches such composition has enhanced penetration for the active such as estradiol (See col. 4, lines 31-36; also col. 3, line 51-64). Carrara also teaches that it is conventional in the art that in order to overcome the barrier of the stratum corneum and facilitate percutanoeous absorption, penetration enhancers are employed (See col. 2, lines 53-60).

Merck Index teaches isopropyl myristate is a penetration enhancer.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ the gel of Carrara and the herein claimed oral dosage forms of methyltestosterone to treat vaginal atrophy in menopausal women. It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ methyltestosterone and estradiol in sequential or simultaneous manner.

One of ordinary skill in the art would have been motivated to employ the gel of Carrara and the herein claimed oral dosage forms of methyltestosterone to treat vaginal atrophy in menopausal women. Employing the estradiol gel of Carrara in the method of Kaswan et al. would have been reasonably expected to be effective since the estradiol

gel of Carrara is effectively enhancing the penetration of estradiol when percutaneously administered. Incorporating isopropyl myristate, a well-known penetration enhancer, into Carrara's gel would be considered obvious as selection over the obvious alternative.

One of ordinary skill in the art would have been motivated to administer methyltestosterone and estradiol in sequential or simultaneous manner. The optimization of result effect parameters (e.g., dosing regimens) is obvious as being within the skill of the artisan.

Response to Arguments

Applicant's arguments filed April 8, 2005 averring no motivation being provided by the cited prior arts have been fully considered but they are not persuasive. The instant claims are directed to a method of treating a menopause disorder comprising the administration of estradiol and methyltestosterone. Kaswan's method can be used to treat vaginal gland atrophy (a menopause disorder) in post-menopausal women, see the abstract and claim 1 for example. Combining androgen, estrogen and prolactin as taught in Kaswan is useful in treating such condition. Therefore, motivation to combine the cited prior arts' teachings is provided since Carrara and Merck Index teaches the employment of agents that aids the penetration of the active ingredients, which would be reasonably expected to enhance the effectiveness of the active and increase the bioavailability of the active.

Applicant's arguments filed April 8, 2005 averring teaching away by Kaswan have been fully considered but they are not persuasive. Applicant's arguments are based on the reason that Kaswan's invention requires the administration of prolactin. Examiner notes that the instant claims recite the transitional phrase "comprising". Any additional components can be used and incorporated into the herein claimed method. Therefore, Kaswan does not teach away the herein claimed method.

Applicant's arguments filed April 8, 2005 averring the secondary references' failure to provide motivation to use for estradiol and methyltestosterone have been considered, but are not found persuasive. Carrara teaches a gel composition has enhanced penetration for the active such as estradiol. Merck index teaches isopropyl myristate is a penetration enhancer. Therefore, incorporating a well-known penetration enhancer such as isopropyl myristate into the gel of Carrara that is used for formulating the Kaswan's composition would have been reasonably expected to be effectively enhancing the penetration and absorption of estradiol, absent evidence to the contrary.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (571) 272-0626. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

San-ming Hui
Primary Examiner
Art Unit 1617